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Amendments To The Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-76.(canceled)

77. (previously presented) A composition for local drug delivery comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a monomeric bone-cement component,

wherein the polymeric bone-cement component comprising the anti-resorptive agent is uniformly mixed with the monomeric bone-cement component to effect a polymerization reaction to obtain a polymerized bone-cement matrix,

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agents added to the polymeric bone-cement component does not weaken the bone-cement component or polymerized bone-cement matrix, or

interfere with polymerization reaction of the bone-cement components, and

wherein the polymerization of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agents.

78. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is a bisphosphonate or a pharmaceutically acceptable salt or ester thereof.
79. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is pamidronate or pharmaceutically acceptable salt or ester thereof.
80. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is etidronate or a pharmaceutically acceptable salt or ester thereof.
81. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is alendronate or a pharmaceutically acceptable salt or ester thereof.
82. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is zoledronate or a pharmaceutically acceptable salt or ester thereof.
83. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is gallium fluoride.

84. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is a cholesterol-lowering agent.
85. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is an estrogen-bisphosphonate conjugate.
86. (previously presented) The composition of claim 77, wherein the bone-cement is an acrylic bone-cement or a hydroxyapatite bone-cement.
87. (previously presented) The composition of claim 77, wherein the bone-cement is polymethylmethacrylate and the anti-resorptive agent is pamidronate or a pharmaceutically acceptable salt or ester thereof.
88. (previously presented) The composition of claim 77, wherein the bone-cement is polymethylmethacrylate and the anti-resorptive agent is zoledronate, zoledronic acid, or a pharmaceutically acceptable salt or ester thereof.
89. (previously presented) The composition of claim 77, wherein 65 to about 70 percent of the polymeric bone-cement particles and the anti-resorptive agents have an average diameter of about 25 microns.
90. (previously presented) The composition of claim 77, wherein 30 to about 35 percent of the polymeric bone cement particles and the anti-resorptive agents are about 13 to about 17 microns in diameter.

91. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is present on the outer surface of the polymerized bone-cement matrix, or is uniformly distributed around the surface of the polymerized bone-cement matrix.

92. (previously presented) The composition of claim 77, wherein the anti-resorptive agent is impregnated throughout the polymerized bone-cement matrix after polymerization reaction.

93. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a composite cement,

wherein the anti-resorptive agent is present in an amount that does not compromise the cement's chemical or mechanical

properties but sufficient to prevent loosening of the bone cement from the living bone;

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component, and

wherein the polymerization reaction of the components of the bone-cement does not chemically interfere with or inactivate the anti-resorptive agent.

94. (previously presented) The composition of claim 93, wherein the amount of the anti-resorptive agent is about 0.067 grams to about 6.67 grams per 40 grams of bone cement.
95. (previously presented) The composition of claim 93, wherein the cement is an organic cement and the anti-resorptive agent is pamidronate in an amount from about 3% to 3.5% by weight of the composition.
96. (previously presented) The composition of claim 93, wherein the amount of the anti-resorptive agent is about 0.67 micrograms to about 3.33 milligrams per 40 grams of bone-cement.
97. (previously presented) The composition of claim 93, wherein the amount of the anti-resorptive agent is about 1.34 micrograms to about 0.2 milligrams per 40 grams of bone-cement.

98. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is a bisphosphonate or a pharmaceutically acceptable salt or ester thereof.
99. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is pamidronate or a pharmaceutically acceptable sale or ester thereof.
100. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is etidronate or a pharmaceutically acceptable sale or ester thereof.
101. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is alendronate or a pharmaceutically acceptable sale or ester thereof.
102. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is zoledronate or a pharmaceutically acceptable salt or ester thereof.
103. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is gallium fluoride.
104. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is a cholesterol-lowering agent.
105. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is an estrogen-bisphosphonate conjugate.

106. (previously presented) The composition of claim 93, wherein the bone-cement is an acrylic bone-cement or hydroxyapatite bone-cement.

107. (previously presented) The composition of claim 93, wherein the bone-cement is polymethylmethacrylate and the anti-resorptive agent is pamidronate or a pharmaceutically acceptable salt or ester thereof.

108. (previously presented) The composition of claim 93, wherein the bone-cement is polymethylmethacrylate and the anti-resorptive agent is zoledronate, zoledronic acid, or a pharmaceutically acceptable salt or ester thereof.

109. (previously presented) The composition of claim 93, wherein the anti-resorptive agent is present in an amount that is not toxic to osteoblast while toxic to osteoclasts.

110. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a

composite cement, wherein the anti-resorptive agent is selected from the group consisting of a salt of a Group IIIA element, a cholesterol-lowering agent, a chemotherapeutic agent-bisphosphonate conjugate, and an estrogen bisphosphonate conjugate,

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component, and

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent.

111. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) a mixture comprising an acrylate monomer and a copolymer

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wherein the copolymer comprises (A) an acrylate or methylmethacrylate monomer and (B) an acrylonitrile, butadiene, styrene, vinyl chloride, vinylidene chloride, or vinyl acetate monomer; (2) an inorganic cement; and (3) a composite cement,

wherein the anti-resorptive agent is selected from the group consisting of a salt of a Group IIIA element; a cholesterol-lowering agent; an estrogen-bisphosphonate conjugate; and a bisphosphonate wherein the bisphosphonate is selected from the group consisting of pamidronate; alendronate; risedronate; ibandronate; zoledronate; olpadronate; icandronate; neridronate (6-amino-1-hydroxyxylidene-1, 1 bishphosphonate); dichloromethane bisphosphonic acid; 3-amino-1-hydroxypropane-1,1-bisphosphonic acid; 6-amino-1-hydroxyhexane-1,1-bisphosphonic acid; 4-amino-1-hydroxybutane-1, 1-bisphosphonic acid; 2-(3-pyridyl)-1-hydroxyethane-1,1-bisphosphonic acid; 2-(N-imidazolyl)-1-hydroxyethane-1,1-bisphosphonic acid; 3-(N-pentyI-N-methylamino)-1-hydroxypropane-1,1-bisphosphonic acid; 3-(N-pyrrolidino)-1-hydroxypropane-1,1-bisphosphonic acid; N-cycloheptylaminoethanebisphosphonic acid; S-(p-chlorophenyl) thiomethane-bisphosphonic acid; 4-amino-1-hydroxybutyliden-1, 1-bisphosphonic acid; (7-dihydro-1-pyridine)methane bisphosphonic acid; (7-dihydro-1-pyridine)hydroxymethane bisphosphonic acid; (6-dihydro-2-pyridine)hydroxy-mehanebisphosphonic acid; 2-(6-pyrrolopyridine)-1-hydroxyethane-1,1-bisphosphonic acid; and pharmaceutically acceptable salts and esters thereof,

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component, and

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent.

112. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a composite cement,

wherein the anti-resorptive agent is a bisphosphonate selected from the group consisting of olpadronate;

icandronate; neridronate; 6-amino-1-hydroxyhexane-1,1-bisphosphonic acid; 2-(3-pyridyl)-1-hydroxyethane-1,1-bisphosphonic acid; 2-(N-imidazolyl)-1-hydroxyethane-1,1-bisphosphonic acid; 3-(N-pentyI-N-methylamino)-1-hydroxypropane-1,1-bisphosphonic acid; 3-(N-pyrrolidino)-1-hydroxypropane-1,1-bisphosphonic acid; 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid; (7-dihydro-1-pyridine)methane bisphosphonic acid; (7-dihydro-1-pyridine)hydroxymethane bisphosphonic acid; (6-dihydro-2-pyridine)hydroxy-methanebisphosphonic acid; 2-(6-pyrolopyridine)-1-hydroxyethane-1,1-bisphosphonic acid; and pharmaceutically acceptable salts and esters thereof, and

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component, and

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent.

113. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

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(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a composite cement,

wherein the anti-resorptive agent is a bisphosphonate selected from the group consisting of dichloromethane bisphosphonic acid; N-cycloheptylaminoethanebisphosphonic acid; and S-(p-chlorophenyl) thiomethane-bisphosphonic acid; and pharmaceutically acceptable salts and esters thereof, and

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component,

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent, and

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wherein the anti-resorptive agent is uniformly distributed throughout the polymerized bone-cement by first mixing the polymeric bone-cement component of the bone-cement with the anti-resorptive agent prior to polymerization reaction.

114. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) and organic cement, (2) an inorganic cement, and (3) a composite cement,

wherein the anti-resorptive agent is a bisphosphonate selected from the group consisting of 1-hydroxyethane-1,1-bisphosphonic acid; 3-amino-1-hydroxypropane-1,1-bisphosphonic acid; 4-amino-1-hydroxybutane-1,1-bisphosphonic acid; and pharmaceutically acceptable salts and esters thereof, and

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

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wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component,

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent, and

wherein the anti-resorptive agent is uniformly distributed throughout the polymerized bone-cement by first mixing the polymeric bone-cement component of the bone-cement with the anti-resorptive agent prior to polymerization reaction.

115. (previously presented) A composition for arresting the process of aseptic loosening attributed to osteoclasts comprising:

(a) a mixture comprising an anti-resorptive agent having a particle-size distribution which is about the same or less than that of a polymeric bone-cement component to provide for even distribution of the anti-resorptive particles throughout a polymerized bone-cement matrix after polymerization reaction; and

(b) a bone-cement selected from the group consisting of (1) an organic cement, (2) an inorganic cement, and (3) a composite cement,

wherein the anti-resorptive agent is a bisphosphonate selected from the group consisting of zoledronate, zoledronic acid, and pharmaceutically acceptable salts and esters thereof, and

wherein the anti-resorptive agent is present in an amount that does not compromise the bone cement's chemical or mechanical properties,

wherein the amount of anti-resorptive agent does not weaken the bone-cement component or interfere with polymerization reaction of the bone-cement component, and

wherein the polymerization reaction of the bone cement components does not chemically interfere with or inactivate the anti-resorptive agent.

116. (canceled)

117. (previously presented) The composition of claim 77 produced by the steps of: (a) mixing a polymer component with an anti-resorptive amount of an anti-resorptive agent to form a mixture; and (b) adding a liquid monomer component to the mixture.

118-121. (canceled)

122. (previously presented) The composition of claim 77, wherein the amount of the anti-resorptive agent is about 1 microgram to about 11 grams per 60 grams of bone cement.

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123. (previously presented) The composition of claim 77, wherein the amount of the anti-resorptive agent is about 0.1 grams to about 10 grams per 60 grams of bone cement.

124. (previously presented) The composition of claim 77, wherein the amount of the anti-resorptive agent is about 0.5 grams per 60 grams of bone cement.

125. (previously presented) The composition of claim 77, wherein the amount of the anti-resorptive agent is about 1 microgram to about 5 milligrams per 60 grams of bone cement.